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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/045,674	10/25/2001	Robert C. Ladner	D2033-708931	2458
37462	7590	04/27/2011	EXAMINER	
LANDO & ANASTASI, LLP ONE MAIN STREET, SUITE 1100 CAMBRIDGE, MA 02142				BOESEN, CHRISTIAN C
ART UNIT		PAPER NUMBER		
1636				
NOTIFICATION DATE			DELIVERY MODE	
04/27/2011			ELECTRONIC	

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

docketing@LALaw.com
gengelson@LALaw.com

Office Action Summary	Application No.	Applicant(s)
	10/045,674	LADNER ET AL.
	Examiner	Art Unit
	CHRISTIAN BOESN	1636

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) Responsive to communication(s) filed on 28 January 2011.

2a) This action is **FINAL**. 2b) This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4) Claim(s) 227-234,240,243 and 248-263 is/are pending in the application.

4a) Of the above claim(s) 248-262 is/are withdrawn from consideration.

5) Claim(s) _____ is/are allowed.

6) Claim(s) 227-234,240,243 and 263 is/are rejected.

7) Claim(s) _____ is/are objected to.

8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9) The specification is objected to by the Examiner.

10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) All b) Some * c) None of:

1. Certified copies of the priority documents have been received.
2. Certified copies of the priority documents have been received in Application No. _____.
3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) Notice of References Cited (PTO-892)

2) Notice of Draftsperson's Patent Drawing Review (PTO-948)

3) Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date 03/07/2011 and 04/08/2011

4) Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.

5) Notice of Informal Patent Application

6) Other: _____.

DETAILED ACTION

This Final Office Action is responsive to the communication received 01/28/2011.

Previous Rejections and/or Objections

Any objections and/or rejections raised in the previous Office Action but not reiterated below are considered to have been withdrawn in view of the Applicant's amendments filed on 01/28/2011.

Claim Rejections - 35 USC § 103 - Maintained

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. § 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.
5. Secondary considerations (objective evidence of nonobviousness): a) commercial success; b) long felt need; c) evidence of unexpected results; d) skepticism of experts; and e) copying.

Common Ownership of Claimed Invention Presumed

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the Examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the Examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 227-234, 240 and 243 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pini (08/21/1998) Journal of Biological Chemistry volume 273 pages 21769 to 21776 in view of Stewart (02/01/1993) Journal of Experimental Medicine volume 177 pages 409 to 418 and Yang (1995) Journal of Molecular Biology volume 254 pages 392 to 403 as evidenced by Tomlinson (10/05/1992) Journal of Molecular Biology volume 227 pages 776 to 798 and Brezinschek (05/1997) Journal of Clinical Investigation volume 99 pages 2488 to 2501.

Applicant's claimed invention is generally directed to a library of polypeptides that include portions related to antibody regions VH CDR1 and VH CDR2 sequences. The Applicant's invention involves the specific sequences -X₁-Y-X₂-M-X₃- (SEQ ID NO:636) and X₄-I-X₅-X₆-S-G-G-X₇-T-X₈-Y-A-D-S-V-K-G- (SEQ ID NO:637), and may also contain VH CDR3, VH 3-23 framework regions and an antibody light chain.

Regarding claims 229 and 231-233 are product-by-process claims and the process recited in this claim is not given any patentable weight. See MPEP 2113, “[T]he lack of physical description in a product-by-process claim makes determination of the patentability of the claim

more difficult, since in spite of the fact that the claim may recite only process limitations, it is the patentability of the product claimed and not of the recited process steps which must be established. We are therefore of the opinion that when the prior art discloses a product which reasonably appears to be either identical with or only slightly different than a product claimed in a product-by-process claim, a rejection based alternatively on either section 102 or section 103 of the statute is eminently fair and acceptable. As a practical matter, the Patent Office is not equipped to manufacture products by the myriad of processes put before it and then obtain prior art products and make physical comparisons therewith.”

With regards to claim 227, Pini and Stewart teach SEQ ID NO 636 (e.g., VH CDR1 coding for -X₁-Y-X₂-M-X₃-) (see results 16, 1 and 53 below and Pini as evidenced by Tomlinson e.g., antibody DP-47, see Figure 2b). Compared to SEQ ID NO 637 (e.g., VH CDR2 coding for X₄-I-X₅-X₆-S-G-G-X₇-T-X₈-Y-A-D-S-V-K-G-) Pini teaches differences are X₄ = A and X₆ = G (e.g., underlined in result 16 below) and Pini teaches the difference is the first G = S (e.g., clones H10 and L19, see Pini, Table II positions 50 and 52) and Pini teaches the entire VH CDR2 coding for X₄-I-X₅-X₆-S-G-G-X₇-T-X₈-Y-A-D-S-V-K-G- other than X₄ = A and X₆ as described above. Steward teaches the difference is X₆ = G (e.g., underlined in result 1 below) and Steward teaches differences are the first G = S and T = I (e.g., underlined in result 53 below) and Steward teaches the entire VH CDR2 coding for X₄-I-X₅-X₆-S-G-G-X₇-T-X₈-Y-A-D-S-V-K-G- other than X₆, the first G and T as described above, thus, in five sequences containing SEQ ID NO 636 and sequences similar to SEQ ID NO 637 Pini and Stewart teach that in VH CDR2 X₄ can be A, S, G or Y and X₆ can be G or S meeting the claim limitations of X₄ and X₆ in SEQ ID NO 637.

Wang teaches saturation mutagenesis of antibody CDRs including VH CDR1 and VH CDR2
(see Abstract).

This page gives you Search Results detail for the Application 10045674 and Search Result 20100916_173349_us-10-045-674d-63614x637.rup.

[Go Back to previous page](#)

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OM protein - protein search, using sw model

Run on: September 16, 2010, 18:21:31 ; Search time 79 Seconds
(without alignments)
1722.987 Million cell updates/sec

Title: US-10-045-674D-63614X637
Perfect score: 95
Sequence: 1 **XYXMXXXXXXXXXXXXXXXXXXXXXXXSGGXTXYADSVKG 36**

Scoring table: BLOSUM62DX
Gapop 10.0 , Gapext 0.1

Searched: 11627486 seqs, 3757527982 residues

Total number of hits satisfying chosen parameters: 11627486

Minimum DB seq length: 0
Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%
Maximum Match 100%
Listing first 150 summaries

Database : UniProt_201006:*

1: uniprot_sprot:*

2: uniprot_trembl:*

SUMMARIES

%

Result No.	Query Score	Match	Length	DB	ID	Description
1	95	100.0	90	2	A2NWX0_HUMAN	A2nwx0 SubName: Fu
2	95	100.0	99	2	A2NWW8_HUMAN	A2nww8 SubName: Fu
3	95	100.0	100	2	A2NWW7_HUMAN	A2nww7 SubName: Fu
4	95	100.0	101	2	A2NWW6_HUMAN	A2nww6 SubName: Fu
5	95	100.0	103	2	A2NWW9_HUMAN	A2nww9 SubName: Fu
6	95	100.0	105	2	A2NWW4_HUMAN	A2nww4 SubName: Fu
7	95	100.0	106	2	A2NWW5_HUMAN	A2nww5 SubName: Fu
8	95	100.0	106	2	A2NWX1_HUMAN	A2nwx1 SubName: Fu
9	95	100.0	110	2	A2NWW2_HUMAN	A2nww2 SubName: Fu

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10	95	100.0	110	2	A2NWW3_HUMAN	A2nww3 SubName: Fu
11	95	100.0	111	2	A2NWX2_HUMAN	A2nwx2 SubName: Fu
12	95	100.0	113	2	A2NWW1_HUMAN	A2nww1 SubName: Fu
13	95	100.0	121	2	A2KUC3_HUMAN	A2kuc3 SubName: Fu
14	95	100.0	131	2	A2NZ55_HUMAN	A2nz55 SubName: Fu
15	95	100.0	161	2	A2NUT3_HUMAN	A2nut3 SubName: Fu
16	95	100.0	238	2	A2KBB9_HUMAN	A2kbb9 SubName: Fu
17	95	100.0	238	2	A2KBC2_HUMAN	A2kbc2 SubName: Fu
18	95	100.0	238	2	A2KBC3_HUMAN	A2kbc3 SubName: Fu
19	95	100.0	238	2	A2KBC4_HUMAN	A2kbc4 SubName: Fu
20	95	100.0	238	2	A2KBC5_HUMAN	A2kbc5 SubName: Fu
21	95	100.0	238	2	A2KBC6_HUMAN	A2kbc6 SubName: Fu
22	95	100.0	238	2	A2KBC7_HUMAN	A2kbc7 SubName: Fu
23	95	100.0	238	2	A2KBC8_HUMAN	A2kbc8 SubName: Fu
24	95	100.0	244	2	A2J422_HUMAN	A2j422 SubName: Fu
25	92	96.8	112	2	Q9HCC1_HUMAN	Q9hcc1 SubName: Fu
26	91	95.8	117	1	HV303_HUMAN	P01764 RecName: Fu
27	91	95.8	121	2	Q9UL71_HUMAN	Q9ul71 SubName: Fu
28	91	95.8	584	2	Q6INK3_XENLA	Q6ink3 SubName: Fu
29	91	95.8	589	2	Q5XHD5_XENLA	Q5xhd5 SubName: Fu
30	91	95.8	593	2	Q6INM5_XENLA	Q6inm5 SubName: Fu
31	90	94.7	96	2	D2I8G8_AILME	D2i8g8 SubName: Fu
32	87	91.6	117	2	D3ZJW6_RAT	D3zjw6 SubName: Fu
33	87	91.6	120	1	HV321_HUMAN	P01782 RecName: Fu
34	87	91.6	128	2	A2KD62_LAMGL	A2kd62 SubName: Fu
35	87	91.6	128	2	A2KD64_LAMGL	A2kd64 SubName: Fu
36	86	90.5	98	2	A2J1N2_HUMAN	A2j1n2 SubName: Fu
37	86	90.5	117	2	A2NTS3_MOUSE	A2nts3 SubName: Fu
38	86	90.5	117	2	D3ZF20_RAT	D3zf20 SubName: Fu
39	86	90.5	118	2	D3ZE00_RAT	D3ze00 SubName: Fu
40	86	90.5	118	2	D4A6W2_RAT	D4a6w2 SubName: Fu
41	86	90.5	120	2	D3ZIT2_RAT	D3zit2 SubName: Fu
42	86	90.5	136	2	D4ACV5_RAT	D4acv5 SubName: Fu
43	86	90.5	138	2	A2NV20_MOUSE	A2nv20 SubName: Fu
44	86	90.5	467	2	Q4VBH1_RAT	Q4vhb1 SubName: Fu
45	86	90.5	475	2	Q6MZQ6_HUMAN	Q6mzq6 SubName: Fu
46	85	89.5	77	2	D2I8T8_AILME	D2i8t8 SubName: Fu
47	85	89.5	109	2	D2I8H4_AILME	D2i8h4 SubName: Fu
48	85	89.5	128	2	A2KD63_LAMGL	A2kd63 SubName: Fu
49	85	89.5	236	2	A2KBC1_HUMAN	A2kbc1 SubName: Fu
50	85	89.5	238	2	A2KBC0_HUMAN	A2kbc0 SubName: Fu
51	85	89.5	470	2	Q68CN4_HUMAN	Q68cn4 SubName: Fu
52	84	88.4	117	1	HVM53_MOUSE	P18524 RecName: Fu
53	83	87.4	97	2	A2NWX4_HUMAN	A2nwx4 SubName: Fu

RESULT 16

A2KBB9_HUMAN

ID A2KBB9_HUMAN Unreviewed; 238 AA.

AC A2KBB9;

DT 20-FEB-2007, integrated into UniProtKB/TrEMBL.

DT 20-FEB-2007, sequence version 1.

DT 02-MAR-2010, entry version 13.

DE SubName: Full=Anti-(ED-B) scFv;

DE Flags: Fragment;

OS Homo sapiens (Human).

OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;

OC Mammalia; Eutheria; Euarchontoglires; Primates; Haplorrhini;

OC Catarrhini; Hominidae; Homo.

Art Unit: 1636

OX NCBI_TaxID=9606;
 RN [1]
 RP NUCLEOTIDE SEQUENCE.
 RX MEDLINE=98371014; PubMed=9705314; DOI=10.1074/jbc.273.34.21769;
 RA Pini A., Viti F., Santucci A., Carnemolla B., Zardi L., Neri P.,
 RA Neri D.;
 RT "Design and use of a phage display library. Human antibodies with
 RT subnanomolar affinity against a marker of angiogenesis eluted from a
 RT two-dimensional gel.";
 RL J. Biol. Chem. 273:21769-21776(1998).
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 CC -----
 DR EMBL; AJ006111; CAA06862.1; -; mRNA.
 DR IPI; IPI00916434; -.
 DR UniGene; Hs.510635; -.
 DR UniGene; Hs.703932; -.
 DR SMR; A2KBB9; 1-238.
 DR STRING; A2KBB9; -.
 DR HOVERGEN; HBG005814; -.
 DR InterPro; IPR007110; Ig-like.
 DR InterPro; IPR013783; Ig-like_fold.
 DR InterPro; IPR013106; Ig_V-set.
 DR InterPro; IPR003596; Ig_V-set_sub.
 DR Gene3D; G3DSA:2.60.40.10; Ig-like_fold; 2.
 DR Pfam; PF07686; V-set; 2.
 DR SMART; SM00406; IGv; 2.
 DR PROSITE; PS50835; IG_LIKE; 2.
 PE 2: Evidence at transcript level;
 FT NON_TER 1 1
 FT NON_TER 238 238
 SQ SEQUENCE 238 AA; 25145 MW; 7875A9A25E4ED418 CRC64;

 Query Match 100.0%; Score 95; DB 2; Length 238;
 Best Local Similarity 38.9%;
 Matches 14; Conservative 22; Mismatches 0; Indels 0; Gaps 0;

 QY 1 XYXMXXXXXXXXXXXXXXXXXXXXXXXSGGXTXYADSVKG 36
 :::::::::::::::::::::||:||:||:|||||||
 Db 31 SYAMSWVRQAPGKGLEWVSAISGGGSTYYADSVKG 66

RESULT 1

A2NWX0_HUMAN
 ID A2NWX0_HUMAN Unreviewed; 90 AA.
 AC A2NWX0;
 DT 20-FEB-2007, integrated into UniProtKB/TrEMBL.
 DT 20-FEB-2007, sequence version 1.
 DT 23-MAR-2010, entry version 13.
 DE SubName: Full=VH-3 family (VH26)D/J protein;
 DE Flags: Fragment;
 GN Name=VH-3 family (VH26)D/J;
 OS Homo sapiens (Human).
 OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
 OC Mammalia; Eutheria; Euarchontoglires; Primates; Haplorrhini;
 OC Catarrhini; Hominidae; Homo.

Art Unit: 1636

OX NCBI_TaxID=9606;
 RN [1]
 RP NUCLEOTIDE SEQUENCE.
 RC TISSUE=Peripheral blood;
 RX MEDLINE=93147730; PubMed=8426111; DOI=10.1084/jem.177.2.409;
 RA Stewart A.K., Huang C., Stollar B.D., Schwartz R.S.;
 RT "High-frequency representation of a single VH gene in the expressed
 RT human B cell repertoire.";
 RL J. Exp. Med. 177:409-418 (1993).
 CC -----
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 CC -----
 DR EMBL; X67069; CAA47454.1; -; Genomic_DNA.
 DR IPI; IPI00827788; -.
 DR PIR; S24248; S24248.
 DR SMR; A2NWX0; 26-90.
 DR STRING; A2NWX0; -.
 DR H-InvDB; HIX0176352; -.
 DR InterPro; IPR013783; Ig-like_fold.
 DR InterPro; IPR013106; Ig_V-set.
 DR InterPro; IPR003596; Ig_V-set_sub.
 DR Gene3D; G3DSA:2.60.40.10; Ig-like_fold; 1.
 DR Pfam; PF07686; V-set; 1.
 DR SMART; SM00406; IGV; 1.
 PE 4: Predicted;
 FT NON_TER 1 1
 FT NON_TER 90 90
 SQ SEQUENCE 90 AA; 9846 MW; EBF8E62181A223A2 CRC64;

 Query Match 100.0%; Score 95; DB 2; Length 90;
 Best Local Similarity 38.9%;
 Matches 14; Conservative 22; Mismatches 0; Indels 0; Gaps 0;

 Qy 1 XYXMXXXXXXXXXXXXXXXXXXXXXXXSGGXTXYADSVKG 36
 :|:|:||||:||||:||||:||||:|:
 Db 30 SYAMSWVRQRPKGLEWVSGISGSGGSTYYADSVKG 65

RESULT 53

A2NWX4_HUMAN
 ID A2NWX4_HUMAN Unreviewed; 97 AA.
 AC A2NWX4;
 DT 20-FEB-2007, integrated into UniProtKB/TrEMBL.
 DT 20-FEB-2007, sequence version 1.
 DT 02-MAR-2010, entry version 10.
 DE SubName: Full=VH-7 family (N54P3)D/J protein;
 DE Flags: Fragment;
 GN Name=VH-7 family (N54P3)D/J;
 OS Homo sapiens (Human).
 OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
 OC Mammalia; Eutheria; Euarchontoglires; Primates; Haplorrhini;
 OC Catarrhini; Hominidae; Homo.
 OX NCBI_TaxID=9606;
 RN [1]
 RP NUCLEOTIDE SEQUENCE.
 RC TISSUE=Peripheral blood;
 RX MEDLINE=93147730; PubMed=8426111; DOI=10.1084/jem.177.2.409;

Art Unit: 1636

RA Stewart A.K., Huang C., Stollar B.D., Schwartz R.S.;
RT "High-frequency representation of a single VH gene in the expressed
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RL J. Exp. Med. 177:409-418(1993).
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CC -----
DR EMBL; X67073; CAA47458.1; -; Genomic_DNA.
DR PIR; S24252; S24252.
DR SMR; A2NWX4; 1-97.
DR STRING; A2NWX4; -.
DR InterPro; IPR007110; Ig-like.
DR InterPro; IPR013783; Ig-like_fold.
DR InterPro; IPR013106; Ig_V-set.
DR InterPro; IPR003596; Ig_V-set_sub.
DR Gene3D; G3DSA:2.60.40.10; Ig-like_fold; 1.
DR Pfam; PF07686; V-set; 1.
DR SMART; SM00406; IGV; 1.
DR PROSITE; PS50835; IG_LIKE; 1.
PE 4: Predicted;
FT NON_TER 1 1
FT NON_TER 97 97
SQ SEQUENCE 97 AA; 10922 MW; 902F4C915457D3F3 CRC64;

Query Match 87.4%; Score 83; DB 2; Length 97;
Best Local Similarity 33.3%;
Matches 12; Conservative 22; Mismatches 2; Indels 0; Gaps 0;

Qy 1 XYXMXXXXXXXXXXXXXXXXXXXXXXXSGGXTXYADSVKG 36
:|:|:||||:||||:||||:|:|:|:|:|:
Db 8 DYYMSWIRQAPGKGLEWVSYI~~SSG~~STIYYADSVKG 43

With regards to claims 228, (230 and 240) and (234 and 243), Pini teaches a library of antibodies containing a VH CDR3 e.g., a human antibody library (see Abstract), a library of antibodies containing an immunoglobulin light chain e.g., a human antibody library (see Abstract and page 21770 left top) and a library of antibodies containing VH 3-23 framework regions e.g., the VH is DP-47 (see page 21770 left top) and DP-47 contains the VH 3-23 framework regions as evidenced by Brezinschek (see Brezinschek, Abstract).

With regards to claims 228 and (230 and 240), Stewart teaches a library of antibodies containing a VH CDR3 e.g., antibodies produced by circulating B cells of four individuals and

two patients (see Abstract) and a library of antibodies containing an immunoglobulin light chain e.g., antibodies produced by the circulating B cells contain light chains (see Abstract).

With regards to claims 228 and (230 and 240), Yang teaches a library of antibodies containing a VH CDR3 e.g., the library of human antibody b4/12 mutants include a VH CDR3 (see Abstract and Figure 1) and a library of antibodies containing an immunoglobulin light chain e.g., the library of human antibody b4/12 mutants include a light chain (see Abstract and Figure 1).

One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success in arriving at the Applicant's invention as claimed with the above cited references before them. Pini, Stewart and Yang are directed towards libraries of antibody polypeptides that include portions related to antibody regions VH CDR1 and VH CDR2 sequences. Pini and Stewart teach libraries that include polypeptides that code for -X₁-Y-X₂-M-X₃- in the VH CDR1 region and a VH CDR2 region that is almost identical to SEQ ID NO 637. Pini and Stewart teach in VH CDR2 X₄ can be A, G or Y and X₆ can be G or S meeting the claim limitation of X₄ is Y, R, W, V, G or S and X₆ is P or S. One of ordinary skill in the art would have recognized the advantages of using the approach of varying X₄ and X₆ to other residues from known antibodies because Yang teaches that saturation mutagenesis of CDRs, including VH CDR2, can result in an improvement in antibody affinity (see Abstract). Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Claim Rejections - 35 USC § 103 - Necessitated by Amendment

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. § 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.
5. Secondary considerations (objective evidence of nonobviousness): a) commercial success; b) long felt need; c) evidence of unexpected results; d) skepticism of experts; and e) copying.

Common Ownership of Claimed Invention Presumed

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the Examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the Examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 227-234, 240, 243 and 263 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pini (08/21/1998) *Journal of Biological Chemistry* volume 273 pages 21769 to

21776 in view of Stewart (02/01/1993) Journal of Experimental Medicine volume 177 pages 409 to 418 and Yang (1995) Journal of Molecular Biology volume 254 pages 392 to 403 as evidenced by Tomlinson (10/05/1992) Journal of Molecular Biology volume 227 pages 776 to 798 and Brezinschek (05/1997) Journal of Clinical Investigation volume 99 pages 2488 to 2501. This rejection is necessitated by Applicant's amendatory material of "Fab fragments or scFv fragments" to new claim 263.

Applicant's claimed invention is generally directed to a library of polypeptides that include portions related to antibody regions VH CDR1 and VH CDR2 sequences. The Applicant's invention involves the specific sequences -X₁-Y-X₂-M-X₃- (SEQ ID NO:636) and X₄-I-X₅-X₆-S-G-G-X₇-T-X₈-Y-A-D-S-V-K-G- (SEQ ID NO:637), and may also contain VH CDR3, VH 3-23 framework regions and an antibody light chain.

Regarding claims 229 and 231-233 are product-by-process claims and the process recited in this claim is not given any patentable weight. See MPEP 2113, "[T]he lack of physical description in a product-by-process claim makes determination of the patentability of the claim more difficult, since in spite of the fact that the claim may recite only process limitations, it is the patentability of the product claimed and not of the recited process steps which must be established. We are therefore of the opinion that when the prior art discloses a product which reasonably appears to be either identical with or only slightly different than a product claimed in a product-by-process claim, a rejection based alternatively on either section 102 or section 103 of the statute is eminently fair and acceptable. As a practical matter, the Patent Office is not equipped to manufacture products by the myriad of processes put before it and then obtain prior art products and make physical comparisons therewith."

With regards to claim 227, Pini and Stewart teach SEQ ID NO 636 (e.g., VH CDR1 coding for -X₁-Y-X₂-M-X₃-) (see results 16, 1 and 53 below and Pini as evidenced by Tomlinson e.g., antibody DP-47, see Figure 2b). Compared to SEQ ID NO 637 (e.g., VH CDR2 coding for X₄-I-X₅-X₆-S-G-G-X₇-T-X₈-Y-A-D-S-V-K-G-) Pini teaches differences are X₄ = A and X₆ = G (e.g., underlined in result 16 below) and Pini teaches the difference is the first G = S (e.g., clones H10 and L19, see Pini, Table II positions 50 and 52) and Pini teaches the entire VH CDR2 coding for X₄-I-X₅-X₆-S-G-G-X₇-T-X₈-Y-A-D-S-V-K-G- other than X₄ = A and X₆ as described above. Steward teaches the difference is X₆ = G (e.g., underlined in result 1 below) and Steward teaches differences are the first G = S and T = I (e.g., underlined in result 53 below) and Steward teaches the entire VH CDR2 coding for X₄-I-X₅-X₆-S-G-G-X₇-T-X₈-Y-A-D-S-V-K-G- other than X₆, the first G and T as described above, thus, in five sequences containing SEQ ID NO 636 and sequences similar to SEQ ID NO 637 Pini and Stewart teach that in VH CDR2 X₄ can be A, S, G or Y and X₆ can be G or S meeting the claim limitations of X₄ and X₆ in SEQ ID NO 637. Wang teaches saturation mutagenesis of antibody CDRs including VH CDR1 and VH CDR2 (see Abstract).

This page gives you Search Results detail for the Application 10045674 and Search Result 20100916_173349_us-10-045-674d-63614x637.rup.

[Go Back to previous page](#)

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OM protein - protein search, using sw model

Run on: September 16, 2010, 18:21:31 ; Search time 79 Seconds
(without alignments)
1722.987 Million cell updates/sec

Art Unit: 1636

Title: US-10-045-674D-63614X637
 Perfect score: 95
Sequence: 1 XYXMXXXXXXXXXXXXXXXSGGXTXYADSVKG 36

Scoring table: BLOSUM62DX
 Gapop 10.0 , Gapext 0.1

Searched: 11627486 seqs, 3757527982 residues

Total number of hits satisfying chosen parameters: 11627486

Minimum DB seq length: 0
 Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%
 Maximum Match 100%
 Listing first 150 summaries

Database : UniProt_201006:*

1: uniprot_sprot:*

2: uniprot_trembl:*

SUMMARIES

%

Result	Query				Description
No.	Score	Match	Length	DB	ID

1	95	100.0	90	2	A2NWX0_HUMAN	A2nwx0 SubName: Fu
2	95	100.0	99	2	A2NWW8_HUMAN	A2nww8 SubName: Fu
3	95	100.0	100	2	A2NWW7_HUMAN	A2nww7 SubName: Fu
4	95	100.0	101	2	A2NWW6_HUMAN	A2nww6 SubName: Fu
5	95	100.0	103	2	A2NWW9_HUMAN	A2nww9 SubName: Fu
6	95	100.0	105	2	A2NWW4_HUMAN	A2nww4 SubName: Fu
7	95	100.0	106	2	A2NWW5_HUMAN	A2nww5 SubName: Fu
8	95	100.0	106	2	A2NWX1_HUMAN	A2nwx1 SubName: Fu
9	95	100.0	110	2	A2NWW2_HUMAN	A2nww2 SubName: Fu
10	95	100.0	110	2	A2NWW3_HUMAN	A2nww3 SubName: Fu
11	95	100.0	111	2	A2NWX2_HUMAN	A2nwx2 SubName: Fu
12	95	100.0	113	2	A2NWW1_HUMAN	A2nww1 SubName: Fu
13	95	100.0	121	2	A2KUC3_HUMAN	A2kuc3 SubName: Fu
14	95	100.0	131	2	A2NZ55_HUMAN	A2nz55 SubName: Fu
15	95	100.0	161	2	A2NUT3_HUMAN	A2nut3 SubName: Fu
16	95	100.0	238	2	A2KBB9_HUMAN	A2kbb9 SubName: Fu
17	95	100.0	238	2	A2KBC2_HUMAN	A2kbc2 SubName: Fu
18	95	100.0	238	2	A2KBC3_HUMAN	A2kbc3 SubName: Fu
19	95	100.0	238	2	A2KBC4_HUMAN	A2kbc4 SubName: Fu
20	95	100.0	238	2	A2KBC5_HUMAN	A2kbc5 SubName: Fu
21	95	100.0	238	2	A2KBC6_HUMAN	A2kbc6 SubName: Fu
22	95	100.0	238	2	A2KBC7_HUMAN	A2kbc7 SubName: Fu
23	95	100.0	238	2	A2KBC8_HUMAN	A2kbc8 SubName: Fu
24	95	100.0	244	2	A2J422_HUMAN	A2j422 SubName: Fu
25	92	96.8	112	2	Q9HCC1_HUMAN	Q9hcc1 SubName: Fu
26	91	95.8	117	1	HV303_HUMAN	P01764 RecName: Fu
27	91	95.8	121	2	Q9UL71_HUMAN	Q9ul71 SubName: Fu
28	91	95.8	584	2	Q6INK3_XENLA	Q6ink3 SubName: Fu
29	91	95.8	589	2	Q5XHD5_XENLA	Q5xhd5 SubName: Fu
30	91	95.8	593	2	Q6INM5_XENLA	Q6inm5 SubName: Fu
31	90	94.7	96	2	D2I8G8_AILME	D2i8g8 SubName: Fu
32	87	91.6	117	2	D3ZJW6_RAT	D3zjw6 SubName: Fu
33	87	91.6	120	1	HV321_HUMAN	P01782 RecName: Fu
34	87	91.6	128	2	A2KD62_LAMGL	A2kd62 SubName: Fu

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35	87	91.6	128	2	A2KD64_LAMGL	A2kd64 SubName: Fu
36	86	90.5	98	2	A2J1N2_HUMAN	A2j1n2 SubName: Fu
37	86	90.5	117	2	A2NTS3_MOUSE	A2nts3 SubName: Fu
38	86	90.5	117	2	D3ZF20_RAT	D3zf20 SubName: Fu
39	86	90.5	118	2	D3ZE00_RAT	D3ze00 SubName: Fu
40	86	90.5	118	2	D4A6W2_RAT	D4a6w2 SubName: Fu
41	86	90.5	120	2	D3ZIT2_RAT	D3zit2 SubName: Fu
42	86	90.5	136	2	D4ACV5_RAT	D4acv5 SubName: Fu
43	86	90.5	138	2	A2NV20_MOUSE	A2nv20 SubName: Fu
44	86	90.5	467	2	Q4VBL1_RAT	Q4vbl1 SubName: Fu
45	86	90.5	475	2	Q6MZQ6_HUMAN	Q6mzq6 SubName: Fu
46	85	89.5	77	2	D2I8T8_AILME	D2i8t8 SubName: Fu
47	85	89.5	109	2	D2I8H4_AILME	D2i8h4 SubName: Fu
48	85	89.5	128	2	A2KD63_LAMGL	A2kd63 SubName: Fu
49	85	89.5	236	2	A2KBC1_HUMAN	A2kbc1 SubName: Fu
50	85	89.5	238	2	A2KBC0_HUMAN	A2kbc0 SubName: Fu
51	85	89.5	470	2	Q68CN4_HUMAN	Q68cn4 SubName: Fu
52	84	88.4	117	1	HVM53_MOUSE	P18524 RecName: Fu
53	83	87.4	97	2	A2NWX4_HUMAN	A2nwx4 SubName: Fu

RESULT 16

A2KBB9_HUMAN

ID A2KBB9_HUMAN Unreviewed; 238 AA.

AC A2KBB9;

DT 20-FEB-2007, integrated into UniProtKB/TrEMBL.

DT 20-FEB-2007, sequence version 1.

DT 02-MAR-2010, entry version 13.

DE SubName: Full=Anti-(ED-B) scFv;

DE Flags: Fragment;

OS Homo sapiens (Human).

OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;

OC Mammalia; Eutheria; Euarchontoglires; Primates; Haplorrhini;

OC Catarrhini; Hominidae; Homo.

OX NCBI_TaxID=9606;

RN [1]

RP NUCLEOTIDE SEQUENCE.

RX MEDLINE=98371014; PubMed=9705314; DOI=10.1074/jbc.273.34.21769;

RA Pini A., Viti F., Santucci A., Carnemolla B., Zardi L., Neri P.,

RA Neri D.;

RT "Design and use of a phage display library. Human antibodies with

RT subnanomolar affinity against a marker of angiogenesis eluted from a

RT two-dimensional gel.";

RL J. Biol. Chem. 273:21769-21776(1998).

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CC -----

DR EMBL; AJ006111; CAA06862.1; -; mRNA.

DR IPI; IPI00916434; -.

DR UniGene; Hs.510635; -.

DR UniGene; Hs.703932; -.

DR SMR; A2KBB9; 1-238.

DR STRING; A2KBB9; -.

DR HOVERGEN; HBG005814; -.

DR InterPro; IPR007110; Ig-like.

DR InterPro; IPR013783; Ig-like_fold.

DR InterPro; IPR013106; Ig_V-set.

DR InterPro; IPR003596; Ig_V-set_sub.

Art Unit: 1636

```

DR  Gene3D; G3DSA:2.60.40.10; Ig-like_fold; 2.
DR  Pfam; PF07686; V-set; 2.
DR  SMART; SM00406; IGV; 2.
DR  PROSITE; PS50835; IG_LIKE; 2.
PE  2: Evidence at transcript level;
FT  NON_TER      1      1
FT  NON_TER      238     238
SQ  SEQUENCE    238 AA;  25145 MW;  7875A9A25E4ED418 CRC64;

Query Match          100.0%;  Score 95;  DB 2;  Length 238;
Best Local Similarity 38.9%;
Matches 14;  Conservative 22;  Mismatches 0;  Indels 0;  Gaps 0;
Qy      1 XYXMXXXXXXXXXXXXXXXXXXXXXXXSGGXTXYADSVKG 36
       :|:|:||||:||||:|:|||||||
Db      31 SYAMSWVRQAPGKGLEWVSAISGSGSTYYADSVKG 66

```

RESULT 1

A2NWX0_HUMAN

ID A2NWX0_HUMAN Unreviewed; 90 AA.

AC A2NWX0;

DT 20-FEB-2007, integrated into UniProtKB/TrEMBL.

DT 20-FEB-2007, sequence version 1.

DT 23-MAR-2010, entry version 13.

DE SubName: Full=VH-3 family (VH26)D/J protein;

DE Flags: Fragment;

GN Name=VH-3 family (VH26)D/J;

OS Homo sapiens (Human).

OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;

OC Mammalia; Eutheria; Euarchontoglires; Primates; Haplorrhini;

OC Catarrhini; Hominidae; Homo.

OX NCBI_TaxID=9606;

RN [1]

RP NUCLEOTIDE SEQUENCE.

RC TISSUE=Peripheral blood;

RX MEDLINE=93147730; PubMed=8426111; DOI=10.1084/jem.177.2.409;

RA Stewart A.K., Huang C., Stollar B.D., Schwartz R.S.;

RT "High-frequency representation of a single VH gene in the expressed human B cell repertoire.";

RL J. Exp. Med. 177:409-418(1993).

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CC -----

DR EMBL; X67069; CAA47454.1; -; Genomic_DNA.

DR IPI; IPI00827788; -.

DR PIR; S24248; S24248.

DR SMR; A2NWX0; 26-90.

DR STRING; A2NWX0; -.

DR H-InvDB; HIX0176352; -.

DR InterPro; IPR013783; Ig-like_fold.

DR InterPro; IPR013106; Ig_V-set.

DR InterPro; IPR003596; Ig_V-set_sub.

DR Gene3D; G3DSA:2.60.40.10; Ig-like_fold; 1.

DR Pfam; PF07686; V-set; 1.

DR SMART; SM00406; IGV; 1.

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RESULT 53

A2NWX4_HUMAN
ID A2NWX4_HUMAN Unreviewed; 97 AA.
AC A2NWX4;
DT 20-FEB-2007, integrated into UniProtKB/TrEMBL.
DT 20-FEB-2007, sequence version 1.
DT 02-MAR-2010, entry version 10.
DE SubName: Full=VH-7 family (N54P3)D/J protein;
DE Flags: Fragment;
GN Name=VH-7 family (N54P3)D/J;
OS Homo sapiens (Human).
OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC Mammalia; Eutheria; Euarchontoglires; Primates; Haplorrhini;
OC Catarrhini; Hominidae; Homo.
OX NCBI_TaxID=9606;
RN [1]
RP NUCLEOTIDE SEQUENCE.
RC TISSUE=Peripheral blood;
RX MEDLINE=93147730; PubMed=8426111; DOI=10.1084/jem.177.2.409;
RA Stewart A.K., Huang C., Stollar B.D., Schwartz R.S.;
RT "High-frequency representation of a single VH gene in the expressed
RT human B cell repertoire.";
RL J. Exp. Med. 177:409-418(1993).
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CC -----
DR EMBL; X67073; CAA47458.1; -; Genomic_DNA.
DR PIR; S24252; S24252.
DR SMR; A2NWX4; 1-97.
DR STRING; A2NWX4; -.
DR InterPro; IPR007110; Ig-like.
DR InterPro; IPR013783; Ig-like_fold.
DR InterPro; IPR013106; Ig_V-set.
DR InterPro; IPR003596; Ig_V-set_sub.
DR Gene3D; G3DSA:2.60.40.10; Ig-like_fold; 1.
DR Pfam; PF07686; V-set; 1.
DR SMART; SM00406; IGV; 1.
DR PROSITE; PS50835; IG_LIKE; 1.
PE 4: Predicted;
FT NON_TER 1 1
FT NON_TER 97 97
SQ SEQUENCE 97 AA; 10922 MW; 902F4C915457D3F3 CRC64;

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Query Match           87.4%;  Score 83;  DB 2;  Length 97;
Best Local Similarity 33.3%;
Matches 12;  Conservative 22;  Mismatches 2;  Indels 0;  Gaps 0;

Qy      1 XYXMXXXXXXXXXXXXXXXXXXXXXXXSXXGGXTXYADSVKG 36
        ::|:|:||||:||||:|:||| : :|||||||
Db      8 DYYMSWIRQAPGKGLEWVSYISSLGTTIYYADSVKG 43

```

With regards to claims 228, (230 and 240), (234 and 243) and 263, Pini teaches a library of antibodies containing a VH CDR3 e.g., a human antibody library (see Abstract), a library of antibodies containing an immunoglobulin light chain e.g., a human antibody library (see Abstract and page 21770 left top), the antibody is an scFv fragment (see page 21770 left top and Figure 1A-B) and a library of antibodies containing VH 3-23 framework regions e.g., the VH is DP-47 (see page 21770 left top) and DP-47 contains the VH 3-23 framework regions as evidenced by Brezinschek (see Brezinschek, Abstract).

With regards to claims 228 and (230 and 240), Stewart teaches a library of antibodies containing a VH CDR3 e.g., antibodies produced by circulating B cells of four individuals and two patients (see Abstract) and a library of antibodies containing an immunoglobulin light chain e.g., antibodies produced by the circulating B cells contain light chains (see Abstract).

With regards to claims 228 and (230 and 240), Yang teaches a library of antibodies containing a VH CDR3 e.g., the library of human antibody b4/12 mutants include a VH CDR3 (see Abstract and Figure 1) and a library of antibodies containing an immunoglobulin light chain e.g., the library of human antibody b4/12 mutants include a light chain (see Abstract and Figure 1).

One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success in arriving at the Applicant's invention as claimed with the above cited references before them. Pini, Stewart and Yang are directed towards libraries of antibody polypeptides that include portions related to antibody regions VH CDR1 and VH CDR2 sequences. Pini and Stewart teach libraries that include polypeptides that code for -X₁-Y-X₂-M-X₃- in the VH CDR1 region and a VH CDR2 region that is almost identical to SEQ ID NO 637. Pini and Stewart teach in VH CDR2 X₄ can be A, G or Y and X₆ can be G or S meeting the claim limitation of X₄ is Y, R, W, V, G or S and X₆ is P or S. One of ordinary skill in the art would have recognized the advantages of using the approach of varying X₄ and X₆ to other residues from known antibodies because Yang teaches that saturation mutagenesis of CDRs, including VH CDR2, can result in an improvement in antibody affinity (see Abstract). Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Discussion and Answer to Argument

The Applicant argues that the amendment removing the words "captured" and "isolated" from claims 229 and 231-233 remove the product-by-process language from the claims (Reply, page 8 line 10).

A library of antibodies is a product claim. A library of antibodies wherein said VH CDR3 is from the CDR3 region of an immunoglobulin gene from a B cell is a product-by-process claim. Antibody libraries can be derived from natural sources, generated synthetically or a combination of both methods. In this situation, the method by which the antibody library is

generated has no patentable weight because identical antibody libraries can be generated using different methods.

The Applicant argues the reference individually stating that neither Pini nor Steward nor Yang teach an antibody library including SEQ ID NOS 636 and 637 (Reply, page 9 line 20).

The Applicant is directed to the body of the rejection above for detailed discussion of how the combination of the cited references teaches all elements and renders the instant claimed invention obvious.

The Applicant argues the reference individually stating that neither Pini nor Steward provide a teaching, suggestion or motivation to generate an antibody library including SEQ ID NOS 636 and 637 (Reply, page 10 line 17).

Steward teaches variation in naturally obtained antibodies. CDR regions in antibodies are "hot-spots" that undergo extensive mutagenesis in response to activation of the immune system. Pini teaches starting with a naturally obtained antibody and randomly generating mutations in CDR regions. Yang teaches CDR walking mutagenesis where one CDR is randomly mutated and the highest affinity mutant is selected and fixed with the selected residues when a second CDR is randomly mutated. Phage display libraries have a limited size, for example two of Yang's libraries have a size of 2×10^8 and 4×10^8 (see Yang, page 401 right top). It is obvious to analyze information from naturally occurring antibodies or antibodies selected following CDR mutagenesis to restrict the variation in amino acids given the limits of phage display library size.

The Applicant argues the reference individually and inaccurately argues that Pini teaches away from restrict the variation in amino acids because Pini teaches random mutagenesis of CDRs (Reply, page 11 line 3).

Random mutagenesis and restricting the variation in amino acids are not mutually exclusive. Yang teaches CDR walking mutagenesis where one CDR is randomly mutated and the highest affinity mutant is selected and fixed with the selected residues when a second CDR is randomly mutated.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

If Applicants should amend the claims, a complete and responsive reply will clearly identify where support can be found in the disclosure for each amendment. Applicants should point to the page and line numbers of the application corresponding to each amendment, and provide any statements that might help to identify support for the claimed invention (e.g., if the amendment is not supported in *ipsis verbis*, clarification on the record may be helpful). Should Applicants present new claims, Applicants should clearly identify where support can be found in the disclosure.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to CHRISTIAN BOESEN whose telephone number is 571-270-1321. The Examiner can normally be reached on Monday-Friday 9:00 AM to 5:00 PM.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Ardin Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Christian Boesen/
Examiner, Art Unit 1636

/Ardin Marschel/

Supervisory Patent Examiner, Art Unit 1636